

Applicant : Michael J. Detm al.  
Serial No. : 09/536,087  
Filed : March 24, 2000  
Page : 4

Attorney's Docket No.: 10287-051001 / MGH 1470.0

### REMARKS

Claims 2-5, 8-12 and 24-52 have been cancelled without prejudice. Applicants reserve the right to pursue the subject matter of the cancelled claims in one or more continuing or divisional applications. Claims 1, 6 and 7 have been amended and new claims 53-74 have been added. The amendments and new claims are supported throughout the application as filed, e.g., at page 17, line 29 to page 19, line 19; and page 40, lines 1-19. (These pages were amended by the preliminary amendment filed on July 20, 2001, merely to insert SEQ ID NO identifiers for the sequences disclosed in the application as filed). No new matter has been added. The new claims are encompassed by Group I of the restriction requirement.

Responsive to the action mailed September 11, 2001, applicant elects the invention of Group I (claims 1, 6-7, 13-23 and new claims 53 to 74), drawn to a method of treating a subject by administering a TSP-2 polypeptide. The election is made with traverse at least with regard to Groups I and V. Both groups are directed to methods of treatment that are sufficiently related in their steps, modes of operation and reagents needed that they do not impose a serious burden on the Examiner to search and examine. Therefore, Applicants respectfully request that the restriction requirement be withdrawn at least with regard to Groups I and V.

Attached is a marked-up version of the changes being made by the current amendment and a clean copy of all the pending claims. A petition for an extension of time with a check for the required fee is enclosed. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 10287-051001.

Respectfully submitted,

Date: 10/23/01

Laurie Lawrence, Reg. No. 46,593  
Louis Myers  
Reg. No. 35,965

Fish & Richardson P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

**Version with markings to show changes made**

**In the claims:**

Claims 2-5, 8-12 and 24-52 have been cancelled without prejudice.

Claims 1, 6 and 7 have been amended as follows:

--1. (Amended) A method of treating a subject having a disorder characterized by unwanted cell proliferation, the method [comprises increasing TSP-2 activity]comprising administering TSP-2 or a biologically active fragment thereof.

6. (Amended) The method of claim [4]1, wherein the [peptide]fragment comprises the sequence of SEQ ID [NO: ] NO:10 (WSPWAEW).

7. (Amended) The method of claim [6]1, wherein the [peptide has]fragment consists of the sequence of SEQ ID [NO: \_\_] NO: 10 (WSPWAEW).--

**Clean Copy Of All Pending Claims Upon Entry Of This Amendment**

1. A method of treating a subject having a disorder characterized by unwanted cell proliferation, the method comprising administering TSP-2 or a biologically active fragment thereof.
6. The method of claim 1, wherein the fragment comprises the sequence of SEQ ID NO:10 (WSPWAEW).
7. The method of claim 1, wherein the fragment consists of the sequence of SEQ ID NO: 10 (WSPWAEW).
13. The method of claim 1, wherein the disorder is characterized by pre-cancerous, cancerous or neoplastic cells, or the presence of a tumour.
14. The method of claim 13, wherein the disorder affects an epithelial tissue.
15. The method of claim 1, wherein the disorder is characterized by unwanted skin cell proliferation.
16. The method of claim 15, wherein the disorder is a squamous cell carcinoma of the skin or a malignant melanoma.
17. The method of claim 1, wherein the disorder is characterized by unwanted prostate cell proliferation.
18. The method of claim 1, wherein the disorder is characterized by benign unwanted skin proliferation in the skin.
19. The method of claim 18, wherein the disorder is psoriasis or papilloma formation.

20. The method of claim 1, further comprising increasing TSP-1 activity.
21. The method of claim 1 or claim 20, further comprising inhibiting VEGF activity.
22. The method of claim 1, further comprising administering a chemotherapeutic agent.
23. The method of claim 22, wherein the chemotherapeutic agent is taxol or carboplatin.
53. The method of claim 1, wherein the fragment is up to 100 amino acids in length.
54. The method of claim 53, wherein the fragment is up to 50 amino acids in length.
55. The method of claim 1, wherein the fragment is at least 50 amino acids in length.
56. The method of claim 1, wherein the fragment is at least 100 amino acids in length.
57. The method of claim 1, wherein the fragment is at least 200 amino acids in length.
58. The method of claim 1, wherein the fragment comprises at least one type I repeat or functional fragment thereof.
59. The method of claim 1, wherein the fragment includes between about 5 to 50 amino acids of a type I repeat.

60. The method of claim 1, wherein the fragment comprises at least one sequence selected from the group of: amino acids 382-429 of SEQ ID NO:2, amino acids 438-490 of SEQ ID NO:2, and amino acids 495-547 of SEQ ID NO:2, or a functional fragment thereof.

61. The method of claim 1, wherein the fragment comprises SEQ ID NO:11.

62. The method of claim 1, wherein the fragment consists of SEQ ID NO:11.

63. The method of claim 1, wherein the fragment comprises a procollagen domain or a functional fragment thereof.

64. The method of claim 63, wherein the fragment comprises SEQ ID NO:6.

65. The method of claim 63, wherein the fragment comprises SEQ ID NO:7.

66. The method of claim 63, wherein the fragment comprises SEQ ID NO:8.

67. The method of claim 63, wherein the fragment comprises SEQ ID NO:9.

68. The method of claim 1, wherein the fragment comprises a fragment of SEQ ID NO:10 at least 4 amino acids in length.

69. A method of treating a subject having a disorder characterized by unwanted cell proliferation, the method comprising administering a polypeptide comprising a TSP-2 type I domain or a functional fragment thereof.

70. The method of claim 69, wherein the fragment is at least 50 amino acids in length.

71. The method of claim 69, wherein the fragment is at least 100 amino acids in length.

72. A method of treating a subject having a disorder characterized by unwanted cell proliferation, the method comprising administering a TSP-2 procollagen region or a biologically active fragment thereof.

73. The method of claim 72, wherein the fragment is at least 50 amino acids in length.

74. The method of claim 72, wherein the fragment is at least 100 amino acids in length.